Brief Summary of the Circulatory System Devices Panel Meeting – October 26, 2011

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on October 26, 2011 to discuss, make recommendations, and vote on information related to PMA P100046 sponsored by AtriCure Inc. for the AtriCure Synergy Ablation System.

The AtriCure Synergy Ablation System is intended to ablate cardiac tissue for the treatment of persistent or longstanding persistent atrial fibrillation in patients who are undergoing open concomitant coronary artery bypass grafting and/or valve replacement or repair.

Panel Deliberations/FDA questions:

The panel noted that the primary safety results were borderline with respect to the pre-specified performance goal. With regard to the primary safety endpoint (the Major Adverse Event, or MAE, rate), the panel felt that it is difficult to determine what can be attributed to the device/ablation procedure versus the primary concomitant procedure. Although not part of the primary safety endpoint, 8 serious adverse events that occurred within the 30-day follow-up period were determined to be related to the AF ablation procedure for a rate of device- or ablation procedure-related serious adverse events of 14.5%. There was a moderate level of concern about this rate, especially when considering the likely confidence bounds. The Panel felt that a robust physician training program would help minimize the rate of ablation procedure-related serious adverse events.

The Panel discussed the primary effectiveness results when the inadequate drug washout, late cardioversions, alternate methods of lesion creation, and current definitions of treatment failure (Modified Effectiveness) were considered and agreed that although this data was interesting, it was a very conservative view of effectiveness. Panelists were convinced that there was an effectiveness signal and believe that there is a reasonable probability of receiving some benefit from the device. As for the data shown on the label the panel agreed that the Modified Effectiveness table could be inserted in the label to provide important context for the effectiveness results and that the effectiveness rate observed in the study per the protocol-specified definitions for success would represent a "best case scenario."

The Panel agreed that while the pivotal clinical study included patients with paroxysmal, persistent, and longstanding persistent AF, the indication proposed by the sponsor, which includes the persistent and longstanding persistent AF population, is appropriate. Such an indication would encompass the patients who would likely receive this treatment in the real world setting. The Panel did not feel it would be appropriate to include paroxysmal AF in the indication statement as this group was not adequately

represented in the ABLATE study. However, the Panel felt that all results, including those for paroxysmal AF subjects, should be reported in the labeling for full disclosure.

The Panel commented on the displayed 12-month (or greater) effectiveness results and agreed that they did seem congruent and did show an adequate durability of the treatment effect. The panel debated the value of data reported for the smaller additional data sets in interpreting outcomes. However, the Panel agreed that the data from the other sources, including the small data sets, should be included in the label. It was suggested that this data could be shown using forest plots.

The Panel commented on the proposed contraindications, warnings, and precautions in the labeling. The Panel suggested that a precaution or warning should be added to the labeling advising against use of the device in the re-operative setting, as this device has not been studied in re-operative patients and re-operation can introduce additional risk (sponsor agreed). Statistical information in the labeling should be revised to be easier to understand as users may not be familiar with reporting using Bayesian statistical terminology. A full disclosure of all outcomes/data should be added to the labeling.

With regard to the Post-Approval Study (PAS), the Panel commented on the difficulty in determining performance goals and added that determination of such goals should consider comparison with patient populations that received the best alternative treatment(s). With regard to a safety goal, the Panel suggested the registry of the Society of Throracic Surgeons (STS) as a good source for obtaining data to be used as a control. The Panel discussed the need for deciding on the proper analytical handling of study subjects who are not followed for the full three years of the PAS (because of death, lost to follow-up, or other reason) in assessing the long-term effectiveness endpoint. The Panel agreed that the data collection should include repeat cardioversions and ablations, multiple procedures, survival, and baseline characteristics. With regard to the question of a Clinical Events Committee (CEC) for the PAS, the Panel unanimously agreed that a CEC is necessary in order to adjudicate the procedure- and device-relatedness of serious adverse events. The Panel commented that rather than setting arbitrary rates of success, an objective of a PAS could be to better characterize rates of performance.

The sponsor as well as the clinical community might benefit from data collected in an IDE registry for patients treated with the device for paroxysmal AF. Such data might be used by the sponsor to expand the indication to paroxysmal AF patients.

The Panel emphasized the importance of a robust PAS and expressed concern that the PAS may not be enrolled since it was difficult to enroll 55 patients in the premarket study. The Panel appealed to the industry, clinical community and FDA to work towards successfully enrolling and executing a well-designed PAS that will address questions unanswered in the premarket setting.

The Panel discussed the ABLATE study results and additional data provided in the Panel pack and during the FDA and Sponsor presentations and whether the overall picture provided a reasonable assurance of safety and effectiveness for the use of the AtriCure Synergy Ablation System for the proposed indication in the intended population. The Panel believed that efficacy has been adequately demonstrated, but that concerns remained regarding safety.

Vote:

Question 1

The Panel voted **5* to 4 to 1 that the data does show** that there is reasonable assurance that the AtriCure Synergy Ablation System is safe for use in patients who meet the criteria specified in the proposed indication.

*The vote was **4 yes** to **4 no** to **1 abstention** the chair broke the tie by voting yes.

Question 2
The Panel voted **9 to 0 that there is reasonable assurance** that the AtriCure Synergy Ablation System is effective for use in patients who meet the criteria specified in the proposed indication.

Question 3
The Panel voted **5 to 3 to 1 that the benefits** of the AtriCure Synergy Ablation System **do outweigh the risks** of the AtriCure Synergy Ablation System for use in the indicated patient population.

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